

REMARKS

Claims 1-22 were pending in the application. Claim 1 has been amended without prejudice to clarify that the hydrophilic polymer is linked to the interferon molecule “predominantly at a single site” on the molecule, thereby forming a substantially homogenous population of conjugate. Thus, upon entry of the present amendment, claims 1-22 will remain pending.

Amendments to and/or cancellation of the claims were done solely for the purpose of expediting prosecution of the present application. Applicants reserve the right to pursue the subject matter of the claims as originally filed in this or a separate application(s). *No new matter has been added to the application.*

Information Disclosure Statement

Applicants appreciate the Examiner's acknowledgement that the Information Disclosure Statement filed on July 19, 2004 was received.

Rejection of Claim 1 Under 35 U.S.C. §112, Second Paragraph

The Examiner rejects claim 1 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner is of the opinion that the phrase "predominantly a single species" is indefinite.

Applicants disagree. However, to expedite prosecution, claim 1 has been amended to clarify that the hydrophilic polymer is linked to the interferon molecule "predominantly at a single site" on the molecule, thereby obviating the rejection. This amendment mirrors the language of claim 39 issued in U.S. Patent No. 6,706,289, the parent of the present application, examined by the present Examiner.

Notwithstanding the above, the second paragraph of 35 U.S.C. §112 requires that the claims particularly point out and distinctly claim the subject matter regarded as the invention. This is satisfied if one of ordinary skill in the art can determine the metes and bounds of the invention. M.P.E.P. §2173.04.

As applied to the present application, the term "single species" was well known in the art at the time of the present application and, thus, the metes and bounds of claim 1 are also clear and definite under 112, second paragraph. Specifically, the term "single species" was well known in the art to mean that each conjugated (*e.g.*, PEGylated) molecule within the composition is conjugated in the same manner (*e.g.*, at the same site or sites on the molecule), thereby forming a homogenous mixture of molecules. For example, as described in Examples 1-6, only one site (the N-terminal amino group), on each Leu-enkephalin molecule is PEGylated (since Leu-enkephalin has only one site available for reaction with the PEG reagent used in Example 1 (*i.e.*, the N-terminus)). Examples 7-12 disclose the preparation, characterization and administration of compositions for delivering Biphalin, wherein two specific sites on each molecule are PEGylated (since Biphalin has only two sites available for PEGylation). Examples

13-19 disclose the preparation, characterization and administration of compositions for delivering insulin, wherein three specific sites on each molecule are PEGylated (since, as would be recognized by one of ordinary skill in the art, the conditions under which the PEG-insulin conjugate was formed in Example 13 produces a conjugate in which all three insulin amino groups will be covalently coupled to PEG).¹ Therefore, not only is the term “single species” well known in the art, but the specification provides several examples of bioactive molecules, including insulin, which are PEGylated in a uniform manner, thereby forming a single species (*i.e.*, homogenous population) of PEGylated molecules.

Accordingly, for at least the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the present rejection.

***Rejection of Claims 1-22 Under Judicially Created
Doctrine of Obviousness-Type Double Patenting***

Claims 1-22 have been rejected under the judicially created doctrine of double patenting over claims 1-39 of U.S. Patent 6,706,289. While in no way acquiescing to the rejection, Applicants are submitting herewith a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), which obviates this rejection.

¹ The number of amino groups on each of the bioactive molecules described in Examples 1-19 that are available for derivatization (*i.e.*, one for leu-enkephalin, two for biphalin and three for insulin) is well known in the art. In addition, the PEGylation reagent used in Examples 1-19 is well known to be selective for amino groups under the reaction conditions described in these Examples (see *e.g.*, PEG reagent catalog from Nektar Therapeutics, Inc., and also U.S. Patent No. 5,672,662) and, as described, was used in sufficient excess to react with all available amino groups.

CONCLUSION

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

Applicants believe no fee is due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. PRJ-006CN from which the undersigned is authorized to draw.

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Respectfully submitted,

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